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| EXAMINER |
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SRIVASTAVA, KAILASH C

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| ART UNIT | PAPER NUMBER |
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1651

DATE MAILED: 08/27/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/669,051

Applicant(s)

FRANANO, NICOLAS F.

Examiner

DR. Kailash C. Srivastava

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 06-05-2002 (Paper Number 9).

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-39 is/are pending in the application.

4a) Of the above claim(s) 13-39 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-12 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____

4) Interview Summary (PTO-413) Paper No(s) _____

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

DETAILED ACTION

1. Applicant's response filed January 9, 2002 (Paper Number 6) to election requirement in Office Action dated September 21, 2001 (paper Number 5) is acknowledged and entered.
2. Applicant's response filed June 05, 2002 (Paper Number 9) to election of species in Office Action dated March 22, 2002 (paper Number 9) is acknowledged and entered.
3. Claims 1-39 are pending.

INFORMATION DISCLOSURE STATEMENT

4. The information disclosure statement filed 02/11/2002 (Paper Number 7) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claims Objection

5. Claims 4-12 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not depend from another multiple dependent claim. See MPEP § 608.02(n).

Restriction/Election

6. Applicant's response to Election of species is still not according to the restriction requirements stated on Page 4, Lines 4-11 of the Office Action dated September 21, 2001 (paper Number 5) and the Office Letter dated March 22, 2002 (paper Number 9) because the applicant has not elected one material between elastin and collagen (See Page 4, Lines 7-8 of the Office Action dated September 21, 2001). However, to avoid further delay in prosecution of this application, the examiner is considering both the materials: elastin and collagen as claimed in Claims 2 and 4-5.

7. Applicant's election with traverse of Group I, Claims 1-12 filed January 9, 2002 (Paper Number 6) in response to election requirement in Office Action dated September 21, 2001 (paper Number 5) is acknowledged.

8. Applicant's election, filed June 05, 2002 (Paper Number 9) of artery, collagenase and

stenosis as species for prosecution of this application in response to Office Action dated March 22, 2002 (paper Number 9) is also acknowledged.

Applicant's traversal is on the ground (s) that a search of all the groups, and specially Groups I, II and V would not place an additional burden on the examiner. This is not found persuasive because of the reasons of record on pages 2-3 in Office action dated September 21, 2001 (Paper Number 5). In addition, the search for each of the distinct inventions of Groups I-V is not co-extensive particularly with regard to the literature search. Further, a reference that would anticipate the invention of one group would not necessarily anticipate or even make obvious another group. Finally, the condition for patentability is different in each case. Thus, it will be an undue burden to examine all of the inventive Groups in one application. Please note that upon further consideration, the election of species requirement with respect to the type of conduit being treated- i.e., those recited in Claim 11 - is hereby withdrawn. However, the election of species requirement concerning the other species groups remain for the reasons of record stated on Page 4, Lines 4-11 of the Office Action dated September 21, 2001 (paper Number 5). Accordingly, the claims have been examined over the art only in so far as they read upon the various elected species (other than the type of conduit being treated-which have been examined in the entirety with respect to those recited in Claim 11).

The restriction requirement is, therefore, still deemed proper and is made FINAL.

Accordingly, Claims 13-39 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

9. Claims 8 and 10 have been examined only to the extent that they relate to elected species (collagenase and stenosis).

10. Claims 1-12 are examined on merits.

Claim Rejections - 35 U.S.C. § 112

11. Following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 2-12 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The phrase, "otherwise degrade" in Claims 2-4 makes those claims indefinite. Applicant is required to clarify the phrase "otherwise degrade".
- While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Applicant has used the term "collagen" in claims 2-3 to mean "collagen" which is the accepted word in the art. The examiner suggests that the applicant replace the term "collagen" with "collagen".
- The phrase "standard *in vitro* tissue digestion assay" in claims 6-7 renders those claims unclear and indefinite because of the word "standard". This term does not clearly define a "standard assay", and therefore, one skilled in the art would not be reasonably apprised of the scope of the invention. The applicant should clearly define the phrase "standard *in vitro* tissue digestion assay".

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

14. Claims 1-8 are rejected under 35 U.S.C. §102(e) as anticipated by Gokeen et al (U.S. Patent 5,116,615).

Claims recite a method to open an obstructed biological conduit by administering a composition comprising either a single or a mixture of enzymes wherein the enzyme (s) digest (s) the "extracellular matrix of obstructing tissue" and in an in-vitro assay, in contrast to a control, the composition exhibits 10-50% higher tissue digestion.

Gokeen et al., disclose a method to relieve obstructive symptoms resulting from benign prostatic hypertrophy by transurethrally injecting a therapeutically effective dosage of a composition comprising hydrolyzing enzymes (Abstract) collagenase and elastase among other proteolytic and non-proteolytic enzymes (Column 2, Lines 30-68). In the said method, the said obstruction is relieved because of the dissolution of the hypertrophied prostatic tissue that causes rectal or urinary (i.e., a biological conduit) obstruction

(Abstract, Column 3, Lines 45-46). Gokeen et al., further disclose an in-vitro assay (Column 42, Line 64 to Column 43, Line 7), wherein guinea pig prostate tissue treated with the said composition comprising enzyme or enzyme mixture is completely digested (up to 100% digestive activity).

Therefore, the reference is deemed to anticipate the cited claims.

Claim Rejections - 35 U.S.C. § 103

15. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. Claims 1-12 are rejected under 35 U.S.C. § 103 (a) as obvious over Gokeen et al (U. S. Patent 5,116,615) in view of Kunz et al (U. S. Patent 6,074,659)., and Singleton et al (Dictionary of Microbiology and Molecular Biology, 1991. John Wiley and Sons, Page 320).

Claims recite a method to open an obstructed biological conduit by administering a composition comprising either a single enzyme or a mixture of enzymes wherein the enzyme (s) digest (s) the "extracellular matrix of obstructing tissue" and in an in-vitro assay, in contrast to a control, the composition exhibits 10-50% higher tissue digestion. The claims further recite that the said composition is administered to a mammal through a catheter to treat stenosis or obstruction of an artery.

As discussed in item 13 *supra*, Gokeen et al., disclose a method to relieve obstructive symptoms resulting from benign prostatic hypertrophy by injecting through transurethral route a therapeutically effective dosage of a composition comprising hydrolyzing enzymes (Abstract) collagenase and elastase among other proteolytic and non-proteolytic enzymes (Column 2, Lines 30-68). In the said method, the said obstruction is relieved because of the dissolution of the hypertrophied prostatic tissue that causes rectal or urinary (i.e., a biological conduit) obstruction (Abstract, Column 3, Lines 45-46). Gokeen et al., further disclose an in-vitro assay (Column 42, Line 64 to Column 43, Line 7), wherein guinea pig prostate tissue treated with the said composition comprising enzyme or enzyme mixture is completely digested (up to 100% dissolution).

Gokeen et al., however, do not disclose that the said composition comprising enzyme or enzyme mixture is administered to a mammal through a catheter to inhibit stenosis or obstruction of an artery.

Kunz et al., disclose a method for stenosis inhibition in a mammalian host, said method comprising administration of a therapeutic dosage of a vascular smooth muscle binding protein that binds to interstitial matrix (i.e., collagen) of the artery wall to inhibit cellular activity thereby reducing or eliminating stenosis (Abstract, Lines 2-5; Column 3, Lines 2-12). Kunz et al., further disclose that the said therapeutic dosage is administered by a catheter (Column 76, Lines 62-63; Claim 13).

Gokeen et al., do not disclose that their therapeutic composition comprised of enzyme or enzyme mixture is a protein. Singleton et al., however, remedy this deficiency because they disclose that enzymes are proteins (Page 320, Column 1, Line 51).

Thus, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Gokeen et al., by administering Gokeen et al.'s enzyme composition with a catheter to inhibit stenosis or relieve arterial obstruction in a mammal because Gokeen et al., teach that an obstructed biological conduit (e.g., rectal or urinary passage) is de-obstructed through administering a composition comprising a single enzyme or a mixture of enzymes, wherein the extracellular matrix (e.g., collagen) responsible for the said obstruction is digested by the said dosage of said composition and Kunz et al., disclose that arterial obstruction or stenosis in a mammal can be reduced or eliminated by injecting a protein through a catheter. Applicant's have recited that an artery is a biological conduit. Therefore, it would be obvious to combine the teachings of all of the above-cited references to obtain a method to open the obstructed artery in a mammal.

One having ordinary skill in the art would have been motivated to administer to a mammal suffering with an obstructed biological conduit, a catheter mediated therapeutically effective dosage of a composition comprising hydrolyzing enzymes collagenase and elastase (which are also proteins per teachings of Singleton et al. Pg 320, Column 1, Line 51) to reduce or eliminate arterial wall stenosis because Gokeen et al., teach that such a composition relieves the obstructive symptoms by digesting the matrix tissue (i.e., collagen) that causes the said obstruction (Abstract, Column 3, Lines 45-46) and Kunz et al., teach that catheter mediated administration of a vascular smooth muscle binding protein reduces

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or eliminates stenosis as well as obstruction of artery by binding the said protein to the arterial wall smooth muscle (Abstract, Lines 2-5; Column 3, Lines 2-12; Column 76, Lines 62-63; Claim 13).

Based on the teachings of above cited prior art references that a therapeutic dosage of a mixture of collagenase and elastase comprising composition overcomes the obstruction of a biological conduit (Gokeen et al., Abstract, Column 3, Lines 45-46) and that catheter mediated administration of a therapeutic dosage of a vascular smooth muscle binding protein that binds to interstitial matrix, i.e., collagen of the artery wall reduces or eliminates stenosis (Kunz et al., Abstract, Lines 2-5; Column 3, Lines 2-12; Column 76, Lines 62-63; Claim 13) and that enzymes are also proteins (Singleton et al., Page 320, Column 1, Line 51), an artisan of ordinary skill would have had a reasonable expectation that a combination of all these methods would result into a method to relieve obstruction of a biological conduit by administering a composition comprising therapeutic dosage of a hydrolyzing enzyme, or a mixture of hydrolyzing enzymes. No patentable invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients. See *In re Sussman*, 1943 C.D. 518; *In re Huellmantel* 139 USPQ 496; *In re Crockett* 126 USPQ 186.

Therefore, the instantly claimed invention would be obvious under 35 U.S.C. § 103(a).

17. No Claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (703) 605-1196. The examiner can normally be reached on Monday-Thursday from 7:30 A.M. to 6:00 P. M. (Eastern Standard Time or Eastern Daylight Saving Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743 Monday through Thursday. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

~~K~~
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Art Unit 1651
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August 21, 2002



CHRISTOPHER R. TATE
PRIMARY EXAMINER